

REMARKS/ARGUMENTS

This is a full and timely response to the final Office action mailed October 28, 2008 and a submission with the Request for Continued Examination submitted herewith.

Applicant thanks Examiners Brown and Richter for a personal interview held on February 24, 2009, the substance of which is summarized below. Further examination and reconsideration in view of the foregoing amendments and following remarks is respectfully solicited.

Non-elected claims 14 – 20 and 47 – 57 have been cancelled without prejudice or disclaimer. Claims 1, 2, 4 – 13, 21 – 25, and 27 – 46 are pending. Claims 1, 8, 21, 22, and 34 are independent.

Rejections Under 35 U.S.C. § 103

Claims 1, 2, 4 – 13, 22 – 25 and 27 - 33 are rejected under 35 U.S.C. §103(a) as being unpatentable over Tuse et al. (US 6,482,799) in view of Araki et al. (US 2003/0203849) and Zhao (US 2003/0228393) further in view of Dykens et al. (US 2003/0105167) and Huth (US 2004/0120916). Claims 34 – 46 are rejected separately on the same references, while claim 21 is rejected separately over Tuse et al. in view of Araki et al, Zhao and Huth.

The present invention relates to an aqueous solution for contact lens care containing cetylpyridinium chloride (CPC), with an upper limit of about 9.5 ppm. When using CPC, selecting the right surfactant is critical or it will inactivate the antimicrobial activity. The non-ionic surfactant POP-POE is effective without reducing the antimicrobial properties of CPC, so the amount of CPC in the solution can be surprisingly low.

Tuse et al teach ophthalmic solutions containing a buffer, a poly(oxyethylene)-poly(oxypropylene) block copolymer, an antibacterial compound, an antifungal compound, an antiviral compound, and an antimicrobial preservative, including CPC among many others. As the examiner concedes, Tuse is silent as to the amount of CPC. Araki et al. was cited to show the use of CPC in low concentration in eye drops. However neither reference, alone or together suggests that CPC forms a superior combination with poly(oxyethylene)-poly(oxypropylene) block copolymers than other surfactants in a contact lens solution. And it would not have been

obvious that the concentration of CPC could be down around 9.5 ppm to 0.1 ppm if used with POP-POE block copolymers in that application.

At the interview, counsel offered to submit comparative data showing that the claimed combination is superior to others containing CPC with different non-ionic surfactants, including TPGS. The Examiner also noted that Araki et al mentions POP-POE block copolymers can function as gelling agents, albeit one among a group of cellulosic gelling agents (rather than as a surfactant). Both of these issue are addressed in 37 CFR 1.132 Declaration by Dr. Zhi-Jian Yu, submitted herewith.

Addressing the latter point first, Araki et al. does not guide one to select POP-POE specifically, and a person of skill would not favor the POP-POE over the cellulosic gelling agents. POP-POE as used in the present invention is significantly below the level that would be required to 'gel'. In fact, we would like to avoid 'gelling' completely. As such, one of ordinary skill in the art would not have looked at the teaching of Araki to formulate a multi-purpose solution.

At gelling concentrations, this would have taught away from the formulation of a MPS. Gelling occurs at very high POP-PEO concentration. For example, the viscosity of a 10% w/v Pluronic F87 solution is only 4 cps. The viscosity of 10% Tetronic 904 is 2.66 cps. Solutions with these viscosities are watery. A gelling solution normally has a viscosity of more than 100 - 10,000cps. Therefore, > 10% w/v of POP-PEO is required as a gelling agent.

POP-POE as a gelling agent has several problems.

- i. Inactivation of CPC antimicrobial activity due to too high POP-PEO concentration. This can also be seen from Table 4. When Pluronic F87 increases from a detergent level of 0.05% to 0.2%, the AME activity decreases to a marginal level as a stand-alone MPS. At the POP-PEO concentration of > 10%, CPC will be inactive as a disinfecting agent.
- ii. It will excessively increase the retention time of CPC on the cornea due to the composition's high viscosity, which would hold the CPC in place over the cornea, causing Corneal toxicity such as cornea staining and irritation.
- iii. When the composition is evaporated during normal usage, a thick film would form in the lens case causing microbes to be trapped underneath the film and separated from the disinfecting solution.

iv. Any gel residue left on a contact lens (it is standard for MPS residue to be left on the lens when it is inserted in the eye) would be too irritating and cytotoxic.

[Yu Decl. ¶¶ 8-11]

The table below contains the results of comparative experiments conducted as described on pages 21 – 25 of the specification. One can see that CPC/POP-POE has greater antimicrobial efficacy than CPC with other surfactants. Pluronic F87 and Tetronic 904 are PPO-PEO surfactants, and cause no noticeable loss in the antimicrobial activity of CPC at the tested concentration. In fact, Pluronic F87 and Tetronic 904 enhanced the activity against *C. albicans* 10231 when compared with no surfactant in solution (although the inventor expects it to decrease above 1% w/w). In contrast, TPGS, Tween 80 and Cremophor-40, which are non-PPO-PEO surfactants, caused almost total loss in antibacterial efficacy. [Yu Decl. ¶ 12]

| | %w/w | %w/w | %w/w | %w/w | %w/w | %w/w |
|----------------------------------|---------------------|--------|--------|--------|--------|--------|
| TPGS | 0.10 | | | | | |
| Tween 80 | 0.10 | | | | | |
| Cremophor 40 | 0.10 | | | | | |
| Pluronic F87 | 0.10 | | | | | |
| Tetronic 904 | 0.10 | | | | | |
| CPC | 0.0004 | 0.0004 | 0.0004 | 0.0004 | 0.0004 | 0.0004 |
| Boric acid | 0.60 | 0.60 | 0.60 | 0.60 | 0.60 | 0.60 |
| Sodium Borate-10H ₂ O | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 |
| NaCl | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 | 0.45 |
| EDTA | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| | Log drops @ 6 hours | | | | | |
| <i>S.marcescens</i> 13880 | >4.38 | 0.15 | -0.01 | 0.07 | >4.38 | >4.38 |
| <i>S.aureus</i> 6358 | >4.42 | 0.11 | 0 | 0.1 | >4.42 | >4.42 |
| <i>P.aeruginosa</i> 9027 | >4.3 | 1.3 | 0.2 | 0.2 | >4.3 | >4.3 |
| <i>C. albicans</i> 10231 | 2.8 | 0 | -0.1 | -0.2 | >4.1 | >4.1 |
| <i>F.solani</i> 30361 | >4.0 | 0.2 | 0.3 | 0.4 | >4.0 | >4.0 |

Finally, the supporting references, Zhao, Dykens et al. and Huth were cited only to show additional components such as taurine, but would not have suggested that the non-ionic surfactant POP-POE can be effective in cleaning a contact lens without reducing the antimicrobial effect of CPC. Accordingly, the present invention would not have been obvious within the meaning of 35 USC 103.

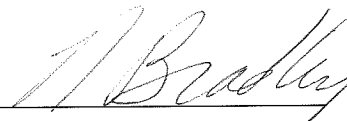
Conclusion

Applicants submit that the present application is in condition for allowance. Favorable reconsideration and withdrawal of the rejections set forth in the above-noted Office Action are requested.

If the Examiner has any comments or suggestions that could place this application in better form, the Examiner is requested to telephone the undersigned attorney at the below-listed number.

If for some reason Applicants have not paid a sufficient fee for this response, please consider this as authorization to charge Deposit Account No. 502317 for any fee which may be due.

Respectfully submitted,

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